DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

Immco Diagnostics, Inc.
Kevin Lawson
VP Regulatory Affairs
9870 Hollingson Rd
Clarence, New York 14031

July 28, 2017

Re: K163177
Trade/Device Name: ImmuLisa Enhanced Gliadin IgA Antibody ELISA, ImmuLisa Enhanced Gliadin IgG Antibody ELISA
Regulation Number: 21 CFR 866.5750
Regulation Name: Radioallergosorbent (RAST) immunological test system
Regulatory Class: Class II
Product Code: MST
Dated: July 5, 2017
Received: July 7, 2017

Dear Kevin Lawson:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR

Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and Part 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely,

Kelly Oliner -S

For
Leonthena R. Carrington, M.S., MBA, MT
Director
Division of Immunology
and Hematology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K163177

Device Name
ImmuLisa™ Enhanced Gliadin IgA Antibody ELISA

ImmuLisa™ Enhanced Gliadin IgG Antibody ELISA

Indications for Use *(Describe)*
Enzyme linked immunosorbent assays (ELISA) for the qualitative or semi-quantitative detection of IgA anti-gliadin antibodies in human serum to aid in the diagnosis of patients with celiac disease or dermatitis herpetiformis in conjunction with other laboratory and clinical findings

Enzyme linked immunosorbent assays (ELISA) for the qualitative or semi-quantitative detection of IgG anti-gliadin antibodies in human serum to aid in the diagnosis of patients with celiac disease or dermatitis herpetiformis in conjunction with other laboratory and clinical findings

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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510(k) Summary

Submitter:	Immco Diagnostics, Inc.
Address:	60 Pineview Dr., Buffalo, NY 14228
Phone Number:	716-691-0091 ext. 110
Contact:	Kevin Lawson
Summary Prepared:	7-27-2017
Device Name:	ImmuLisa™ Enhanced Gliadin IgA Antibody ELISA ImmuLisa™ Enhanced Gliadin IgG Antibody ELISA
Common Name:	Anti-Gliadin IgA or IgG Antibody (AGA) ELISA
Product Code:	Antibodies, Gliadin [MST]
Substantially Equivalent to:	IMMCO Gliadin (AGA) IgA ELISA IMMCO Gliadin (AGA) IgG ELISA

General Description: Celiac Disease (CD) and dermatitis herpetiformis (DH) are autoimmune gastrointestinal and skin disorders that may occur in genetically susceptible individuals triggered by the ingestion of gluten containing grains such as wheat, barley and rye. The classical symptoms of CD include diarrhea, weight loss and malnutrition. Dermatitis herpetiformis is chronic bullous disease characterized by the formation of subepidermal blisters. Only a small percentage of patients with CD present with classical symptoms. The most common serologic tests for the screening of CD or DH are the immunofluorescence method of detecting endomysial antibodies (EMA) and ELISA methods of detecting antibodies to tissue transglutaminase (tTG) and gliadin. The limitation of the EMA and tTG immunoassays is that both immunoassays detect IgA antibodies, hindering identification of IgA deficient patients with CD. IgG gliadin antibody tests are important towards the diagnosis of CD in patients who are IgA deficient. Studies show that 1-2% of the general population is IgA deficient and that the incidence of CD in IgA deficient subjects is significant, hence the need for specific tests. In addition to the native Gliadin assay, Gliadin peptide based assays have shown promising results in addressing the limitations of current assays. This current immunoassay for gliadin antibodies incorporates a native gliadin protein for sensitive and specific detection of IgA or IgG isotype antibodies with a high degree of reliability.

This test is performed as a solid phase immunoassay. Microwells are coated with native purified Gliadin antigen. Controls, calibrators and patient sera are incubated in the antigen coated wells to allow specific antibodies present in the serum to bind to the gliadin antigen. Bound antibodies are detected by adding an enzyme labeled anti-human IgA or IgG conjugate. Specific enzyme substrate (TMB) is then added and the presence of antibodies is detected by a color change that is read by a spectrophotometer at 450 nm. Results are expressed in ELISA units per milliliter (EU/ml) and reported as positive or negative.

Intended Use: Enzyme linked immunosorbent assays (ELISA) for the qualitative or semi-quantitative detection of IgA or IgG anti-gliadin antibodies in human serum to aid in the diagnosis of patients with celiac disease or *dermatitis herpetiformis* in conjunction with other laboratory and clinical findings.

Similarities and Differences: Both kits use native purified Gliadin coated on 96 well plates to detect IgA or IgG Gliadin antibodies with anti-human IgA or IgG conjugate and substrate. Both kits test human serum. Semi-quantitative results are reported in EU/ml for both kits. The Enhanced kit utilizes a HRP anti-human IgA or IgG conjugate and TMB substrate, while the predicate AGA kit uses an alkaline phosphatase IgA or IgG conjugate and pNPP substrate. The Enhanced kit utilizes a 5 point calibrator curve with a borderline / indeterminate range of 20-25 EU/ml while the predicate AGA kit uses a 4 point calibrator curve with a cutoff of 20 units and no borderline range.

Non-clinical Tests:

Method Comparison: Both kits were tested with well-characterized CD and DH subjects and disease controls.

		Predicate AGA IgA		
		Pos	Neg	Total
Immco AGA IgA ELISA	Pos	96	17	113
	Borderline	10	12	22
	Neg	3	262	265
	Total	109	291	400

Disease Associated Specimens:	230	
Disease Control Specimens:	170	
Borderline considered positive		
Positive % Agreement	97.2%	(95% CI 91.6% - 99.3%)
Negative % Agreement	90.0%	(95% CI 85.9% - 93.1%)
Overall % Agreement	92.0%	(95% CI 88.9% - 94.3%)
Borderline considered negative		
Positive % Agreement	88.1%	(95% CI 80.1% - 93.2%)
Negative % Agreement	94.2%	(95% CI 90.6% - 96.5%)
Overall % Agreement	92.5%	(95% CI 89.5% - 94.7%)

		Predicate AGA IgG		
		Pos	Neg	Total
Immco	Pos	190	10	200
AGA IgG	Borderline	9	4	213
ELISA	Neg	6	240	246
	Total	205	254	459

Disease Associated Specimens:	246	
Disease Control Specimens:	213	
Borderline considered positive		
Positive % Agreement	97.1%	(95% CI 93.4% - 98.8%)
Negative % Agreement	94.5%	(95% CI 90.7% - 96.8%)
Overall % Agreement	95.6%	(95% CI 93.4% - 97.2%)
Borderline considered negative		
Positive % Agreement	92.7%	(95% CI 88.0% - 95.7%)
Negative % Agreement	96.1%	(95% CI 92.7% - 98.0%)
Overall % Agreement	94.6%	(95% CI 92.1% - 96.3%)

Cross Reactivity: A total of 456 sera from individuals with other potentially cross-reactive autoimmune disorders were selected to test for gliadin antibodies using the ImmuLisa™ assay. The results appear below.

		Gliadin IgA		Gliadin IgG	
Disease	**n**	**n Pos**	**% Pos**	**n Pos**	**% Pos**
Rheumatoid Arthritis	30	1	3.3%	0	0.0%
Graves' disease	15	1	6.7%	0	0.0%
Hashimoto's thyroiditis	15	0	0.0%	1	6.7%
Systemic lupus erythematosus	30	2	6.7%	3	10.0%
Granulomatosis with polyangiitis	30	0	0.0%	1	3.3%
Systemic sclerosis	30	0	0.0%	0	0.0%
Ulcerative Colitis	25	0	0.0%	1	4.0%
Crohn's disease	25	1	4.0%	2	8.0%
Rubella	20	0	0.0%	0	0.0%
Herpes simplex virus Type 1	20	0	0.0%	0	0.0%
Herpes simplex virus Type 2	20	0	0.0%	3	15.0%
Cytomegalovirus	20	0	0.0%	0	0.0%
Toxoplasmosis	20	0	0.0%	0	0.0%
Lyme disease	36	0	0.0%	3	8.3%
Autoimmune hepatitis	30	0	0.0%	1	3.3%
Primary biliary cirrhosis	50	4	8.0%	3	6.0%
Helicobacter pylori	40	3	7.5%	3	7.5%
Total	456	12	2.6%	21	4.6%

60 Pineview Drive • Buffalo, NY 14228-2120 • USA
Toll free (800) 537-8378 • tel. (716) 691-0091 • fax (716) 691-0466

www.immco.com

Precision

Precision was tested with positive specimens selected throughout the range of the assay. Seven patients were run in duplicate, twice per day for 20 days (n=80 replicates per sample). Assays were run by two operators on two different sets of equipment.

Gliadin IgA

	Mean	Total Imprecision		Within run (Repeatability)		Between days		Between Runs	
S#	EU/ml	SD	CV%	SD	CV%	SD	CV%	SD	CV%
1	3.6	0.4	10.3	0.4	9.9	0.2	6.6	0.1	3.1
2	15.3	0.9	5.6	0.8	5.3	0.6	3.8	0.3	7.1
3	20.2	0.9	4.5	0.8	4.0	0.8	3.9	0.4	2.1
4	23.7	1.4	5.7	1.0	4.1	0.8	3.3	0.9	3.9
5	67.9	2.2	3.2	1.8	2.6	1.3	1.9	1.3	1.9
6	93.2	5.6	5.7	4.9	5.2	4.8	5.1	2.1	2.2
7	143.5	11.0	7.1	9.3	6.4	10.3	7.2	4.4	3.1

Gliadin IgG

	Mean	Total Imprecision		Within run (Repeatability)		Between days		Between Runs	
S#	EU/ml	SD	CV%	SD	CV%	SD	CV%	SD	CV%
1	13.7	1.4	9.9	0.6	4.1	0.6	4.2	1.1	8.0
2	17.4	1.1	6.5	0.6	3.3	0.3	1.8	0.9	5.4
3	19.9	1.2	5.9	0.7	3.3	0.7	3.2	0.7	3.6
4	23.4	1.2	5.3	0.7	2.8	0.5	2.2	1.0	4.4
5	44.8	2.5	5.5	1.8	4.0	0.7	1.6	1.6	3.5
6	96.8	8.5	8.8	3.5	3.6	1.7	1.7	7.6	7.8
7	153.4	13.4	8.7	6.6	4.3	5.1	3.3	11.6	7.6

Qualitative Reproducibility

80 replicates of samples in the low negative range, near the cutoff, in the moderate positive range, and approximately +/- 20% of the assay cutoffs for each AGA isotype were performed to determine qualitative reproducibility. One sample near the cutoff yielded 51.3% and 57.5% agreement on Gliadin IgA and Gliadin IgG respectively, all remaining specimens produced 100% qualitative agreement.

Inter-lot Reproducibility

Inter-lot reproducibility was tested with multiple endogenous specimens selected throughout the range of the assay. Five samples were tested in replicates of 5 on three different lots over the course of five days. There was no recalibration of this equipment over the course of this study. Five samples were tested in replicates of five on three separate assay lots for 5 days.

Gliadin IgA

	Repeatability		Within Lot		Reproducibility	
Mean	SD	CV	SD	CV	SD	CV
9.87	0.36	3.7%	0.74	7.5%	0.74	7.5%
22.56	1.36	6.0%	1.70	7.5%	1.78	7.9%
35.19	0.81	2.3%	2.36	6.7%	2.36	6.7%
77.90	1.60	2.1%	5.72	7.3%	5.88	7.6%
149.72	6.62	4.4%	10.74	7.2%	11.65	7.8%

Gliadin IgG

	Repeatability		Within Lot		Reproducibility	
Mean	SD	CV	SD	CV	SD	CV
16.13	0.59	3.7%	1.49	9.2%	1.49	9.2%
22.59	1.01	4.5%	2.06	9.1%	2.06	9.1%
35.48	1.18	3.3%	3.10	8.7%	3.10	8.7%
87.31	2.69	3.1%	5.37	6.2%	5.66	6.5%
122.87	4.97	4.0%	9.99	8.1%	11.29	9.2%

Inter-site Reproducibility

Site to site reproducibility was tested with multiple endogenous specimens selected throughout the range of the assay. Five samples were tested in replicates of 5 in three different sites over the course of five days. There was no recalibration of this equipment over the course of this study.

Gliadin IgA

	Repeatability		Within Lot		Reproducibility	
Mean	SD	CV	SD	CV	SD	CV
10.00	0.44	4.4%	0.76	7.6%	0.83	8.3%
22.73	0.60	2.7%	1.40	6.2%	2.13	9.4%
47.72	1.36	2.9%	2.87	6.0%	4.10	8.6%
88.38	4.70	5.3%	7.79	8.8%	8.46	9.6%
146.18	5.09	3.5%	11.99	8.2%	12.79	8.8%

Gliadin IgG

	Repeatability		Within Lot		Reproducibility	
Mean	SD	CV	SD	CV	SD	CV
13.99	0.71	5.1%	0.89	6.4%	1.28	9.1%
24.12	0.97	4.0%	1.91	7.9%	2.06	8.5%
33.88	1.35	4.0%	2.36	7.0%	2.36	7.0%
69.97	2.85	4.1%	5.11	7.3%	5.77	8.2%
151.12	5.27	3.5%	10.82	7.2%	13.95	9.2%

Limit of Detection / Limit of Blank / Limit of Quantitation

The limits of blank (LoB) and limits of detection (LoD) were determined based on 60 replicates of the blank and 10 replicates each of 6 low-level (NHS) samples. LoB was determined to be 2.2 EU/ml for IgA and 1.6 EU/ml for IgG. LoD was determined to be 3.6 EU/ml for IgA and 2.8 EU/ml for IgG. The limits of quantitation (LoQ) were determined by testing four low level samples in replicates of four. LoQ was determined to be 7.5 EU/ml for IgA and 4.6 EU/ml for IgG.

Linearity and Recovery

Linearity and recovery were tested by diluting positive specimens through the assay range in equidistant dilutions and comparing actual vs. expected results. The linear range of the assay was determined be 7.5 (LoQ) – 160 EU/ml for IgA and 4.6 (LoQ) – 160 EU/ml for IgG. Results are summarized below.

IgA	Test Range (EU/ml)	Slope (95% CI)	Y-intercept (95% CI)	R^2	% Recovery (Obtnd/Expctd)
	7.4 to 41.6	1.01 (.92 to 1.10)	1.13 (-1.14 to 3.39)	0.9942	92% to 94%
	2.3 to 97.2	1.04 (0.95 to 1.12)	1.45 (-3.18 to 6.08)	0.9935	90% to 96%
	4.7 to 127.4	0.85 (0.79 to 0.91)	2.06 (-3.39 to 7.41)	0.9986	102% to 117%
IgG	Test Range (EU/ml)	Slope (95% CI)	Y-intercept (95% CI)	R^2	% Recovery (Obtnd/Expctd)
	9.0 to 47.0	0.98 (0.88 to 1.08)	0.87 (-2.16 to 3.90)	0.9923	93% to 106%
	12.7 to 116.8	0.98 (0.91 to 1.05)	-1.47 (-6.66 to 3.73)	0.9951	102% to 110%
	58.1 to 147.4	0.98 (0.87 to 1.08)	3.67 (-7.70 to 15.04)	0.9938	98% to 106%

To assess hook effect, dilutions of high positive specimens with results above the 160 EU/ml measuring ranges were tested. Hook effect was not demonstrated in dilution samples as high as ~5,515.8 EU/ml for IgA and 1686.8 EU/ml for IgG within OD range of the microplate reader (~3.5OD).

Interference

Interference was studied by mixing sera with known gliadin antibody levels for each isotype with potentially interfering serum samples and studying deviation from expected results. No significant interference was demonstrated for the following substances at the levels indicated: Hemoglobin (2 g/L), Bilirubin (342 µmol/L), Rheumatoid Factor (100 EU/ml), Triglycerides (37 mmol/L), and Cholesterol (13 mmol/L).

Clinical Study: Sets of clinical samples were tested on the IMMCO Enhanced Gliadin ELISAs. By testing 250 celiac disease and 45 dermatitis herpetiformis along with 456 autoimmune and infectious disease controls following sensitivity and specificity were calculated. IgA deficient CD have been excluded from these calculations.

Borderline / indeterminate results are considered positive:

Celiac Disease	IgA	IgG
Sensitivity	65.6% (95% CI 59.3% - 71.4%)	76.4% (95% CI 70.5% - 81.4%)
Specificity	97.4% (95% CI 95.3% - 98.6%)	95.4% (95% CI 92.9% - 97.1%)

Dermatitis herpetiformis	IgA	IgG
Sensitivity	35.6% (95% CI 22.3% - 51.3%)	57.8% (95% CI 42.2% - 72.0%)
Specificity	97.4% (95% CI 95.3% - 98.6%)	95.4% (95% CI 92.9% - 97.1%)

Borderline / indeterminate results are considered negative:

Celiac Disease	IgA	IgG
Sensitivity	55.6% (95% CI 49.2% - 61.8%)	68.4% (95% CI 62.2% - 74.0%)
Specificity	98.5% (95% CI 96.7% - 99.3%)	96.7% (95% CI 94.5% - 98.1%)

Dermatitis herpetiformis	IgA	IgG
Sensitivity	33.3% (95% CI 20.4% - 49.1%)	55.6% (95% CI 40.1% - 70.0%)
Specificity	98.5% (95% CI 96.7% - 99.3%)	96.7% (95% CI 94.5% - 98.1%)

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60 Pineview Drive ● Buffalo, NY 14228-2120 ● USA
Toll free (800) 537-8378 ● tel. (716) 691-0091 ● fax (716) 691-0466

www.immco.com